

A Phase II Trial of CG 8020 and CG 2505 in Patients with Unresectable or Metastatic Pancreatic Cancer

SCIENTIFIC ABSTRACT

Background

Cancer of the pancreas is the tenth leading cause of cancer in the United States with an estimated incidence of 28,300 new cases in 2000. It is also one of the most lethal malignancies and is currently the fifth leading cause of cancer death with an estimated number of deaths in 2000 similar to the incidence rate. The death rate in pancreatic cancer is exceeded only by lung, colorectal, breast, and prostate cancer. The median survival for pancreatic cancer is 15- 19 months for resectable disease, 6-9 months for locally advanced, unresectable disease, and 3-6 months for metastatic disease. All stages combined have a 1-year survival of 20% and a 5-year survival of approximately 3%. Only one drug, Gemcitabine, is currently approved for unresectable and metastatic disease. In a phase III randomized study comparing Gemcitabine with 5-FU in chemotherapy naïve patients with locally advanced or metastatic adenocarcinoma of the pancreas, Gemcitabine yielded a very modest median overall survival of 5.7 months, 1 year survival of 18%, and improvement of “clinical benefit response”. Alternative therapies with novel mechanisms of action are clearly needed in this disease.

Objectives

This open label Phase II trial will investigate the use of lethally irradiated, allogeneic pancreatic cancer cell lines (CG 8020 and CG 2505, Pancreatic GVAX[®]) genetically engineered to secrete GM-CSF as vaccines for the treatment of unresectable pancreatic cancer. The study is designed to evaluate the clinical and laboratory safety of the vaccine and, as a secondary end point, assess the efficacy of the vaccine as measured by clinical benefit response, survival, progression-free survival, and CA19-9 serum tumor marker levels.

Patient Population

Forty adult patients with unresectable or metastatic adenocarcinoma of the pancreas. Patients may be either chemotherapy naïve or experienced and must have a KPS of ≥ 70 .

Study Design

Phase II multi-center, single arm, multi-dose, open-label trial.

Treatment Plan and Schedule

Patients will receive 6 vaccinations of Pancreatic GVAX[®] at 3 wk intervals.

Dose

Each vaccination will consist of 4-8 intradermal injections of CG 8020 to deliver a total of 2.5×10^8 cells, and 4-8 intradermal injections of CG 2505 to deliver 2.5×10^8 cells for a total of 5×10^8 cells per dose. Combined GM-CSF secretion from both CG 8020 and CG 2505 is estimated to deliver up to 400 µg/vaccine dose/24 hr while tumor vaccine cells are functional (estimated to be approximately 4 days) (Jaffee et al. JCO 2001 19; 1: 145-146).

Dose-Limiting Toxicity

Dose-limiting toxicity (DLT) is defined as any vaccine-related grade 2 or higher allergic toxicity or any vaccine-related grade 3 or 4 toxicity that does not resolve in less than 5 days. If dose-limiting toxicities occur in 30% or more of the patients enrolled in the trial, enrollment will be stopped. Additionally, if two vaccine-related grade 4 toxicities occur, the study will be stopped.

Safety Evaluation

The toxicity data collected will be descriptive, characterized according to the National Cancer Institute Common Toxicity Criteria. Safety parameters will include physical examination, hematology, and serum chemistry. Monitoring for adverse events will be done using an internal and external monitoring system.

Product

Two allogeneic tumor cell lines have been developed from neoplastic tissue harvested from two patients who underwent pancreaticoduodenectomy at The Johns Hopkins Hospital Baltimore, MD. The cell lines CG 2505 (tumor cell line Panc 10.05) and CG 8020 (tumor cell line Panc 6.03) contain the most common *k-ras* mutation at codon 12 found in greater than 90% of pancreatic cancer, as did the original tumor specimens. CG 2505 and CG 8020 were genetically modified to secrete human Granulocyte-macrophage colony-stimulating factor (GM-CSF) by plasmid DNA transfection, (Jaffe et al, Human Gene Therapy 1998; 9:1951-1971; Jaffee et al, Cancer J Sci Am 1998; 4(3): 194-203). The cell lines have been banked and tested under cGMP by Cell Genesys, Inc, Foster City, CA. Clinical lots produced from the banks have been frozen, irradiated and tested. Used in combination, thawed cells from clinical lots of CG 8020 and CG 2505 will be injected as a tumor cell vaccine, Pancreatic GVAX[®].